Single amino acid substitutions on a Japanese cedar pollen allergen (Cry j 1)-derived peptide induced alterations in human T cell responses and T cell receptor antagonism.

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We generated T cell clones specific to a Japanese cedar pollen allergen (Cry j 1) and investigated effects of altered T cell receptor (TCR) ligand on changes of T cell responses. One of these Cry j 1-specific T cell clones established from patients with Japanese cedar pollinosis, ST1.9, recognized an antigenic peptide Cry j 1 p335-346 in the context of HLA-DRA+DRB3*0301 molecules and secreted interleukin-4 dominantly, with a smaller amount of interferon-gamma. ST1.9 represented one of the major T cell clones specific to Cry j 1 in the donor, because a short-term cultured polyclonal T cell line specific to Cry j 1 exhibited the same character as the ST1.9. We synthesized various analog peptides derived from Cry j 1 p335-346 with single amino acid substitutions and determined key residues for interactions between TCR of ST1.9 and HLA-DR molecules. We also analyzed changes in the responses of ST1.9 to Cry j 1 p335-346-derived analog peptides. Of interest was that the substitution of 339threonine to valine resulted in a significant increase in interferon-gamma production, with no remarkable changes either in proliferative response or interleukin-4 production. Analog peptides carrying the substitutions of 339threonine to glycine or glutamine revealed TCR antagonism, without changes in their binding affinities to the DR molecule. Therefore single amino acid substitutions on an allergen peptide carrying the T cell epitope may suppress helper-T-dependent class switch pressure to IgE in B cells either by inducing increased interferon-gamma production or by inhibiting proliferative responses in helper-T cells.

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Immunodominance of seven regions of a major allergen, Cry j 2, of Japanese cedar pollen for T-cell immunity.

Hashiguchi S, Hino K, Taniguchi Y, Kurimoto M, Fukuda K, Ohyama M, Fujiyoshi T, Sonoda S, Nishimura Y, Yamada G, Sugimura K

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The immunodominant regions of the Japanese cedar pollen allergen Cry j 2 for T-cell immunity were determined with whole peripheral blood lymphocytes (PBL) derived from seven allergic patients and three nonallergic subjects. Cry j 2-stimulated T-cell proliferation was inhibited by anti-HLA-DR, but not by anti-HLA-DQ antibody, indicating that the responding T cells recognized the allergen peptides associated with HLA-DR molecules. It was found that seven regions of Cry j 2, i.e., regions corresponding to amino acid numbers 1-26, 70-84, 151-167, 187-203, 252-279, 283-314, and 345-362, were immunodominant for T-cell proliferation. Thus, Cry j 2 bears a limited number of immunodominant regions despite polymorphic features of HLA-DR in the immune system. This suggests the possibility of molecularly designing Cry j 2 antagonists that could downregulate allergic reactions to Japanese cedar pollen.

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